REMARKS

I. Introduction

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

In the specification, paragraphs have been amended to capitalize trademarks.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claims remain under examination in the application, is presented, with an appropriate defined status identifier.

Claims 1-16 are requested to be cancelled. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

Claims 17-37 are new. The new claims are directed to a method of treating a patient for multiple sclerosis comprising administering to the patient an IFN-β mutein having a cysteine at position 17 deleted or replaced by a neutral amino acid at a dosage greater than about 500 mcg up to about 1000 mcg or about 625 mcg. Exemplary support for the new claims can be found in the specification as detailed in the following table.

Exemplary Support for the New Claims in the Application	
Claim	**Exemplary Support**
17	¶ 16; ¶ 17; ¶ 19; ¶ 26; ¶ 34; ¶ 39; ¶ 49; ¶ 52; ¶¶ 60-79; Example 1; and the original claims
18	¶ 62; Example 1; and the original claims
19	¶ 62; Example 1; and the original claims
20	¶ 62; Example 1; and the original claims
21	¶¶ 60-79; Example 1; and the original claims
22	¶¶ 60-79; Example 1; and the original claims
23	¶85; Example 1; and the original claims
24	¶ 86; ¶ 87; ¶ 90; ¶ 91; Example 1; and the original claims
25	¶ 91; Example 1; and the original claims

Exemplary Support for the New Claims in the Application	
Claim	**Exemplary Support**
26	¶ 16; ¶ 17; ¶ 19; ¶ 26; ¶ 34; ¶ 39; ¶ 49; ¶ 52; ¶¶ 60-79; Example 1; and the original claims
27	¶ 16; ¶ 49 and Example 1
28	¶ 16; ¶ 49 and Example 1
29	¶ 16; ¶ 49 and Example 1
30	¶ 62; Example 1; and the original claims
31	¶ 62; Example 1; and the original claims
32	¶ 62; Example 1; and the original claims
33	¶¶ 60-79; Example 1; and the original claims
34	¶¶ 60-79; Example 1; and the original claims
35	¶85; Example 1; and the original claims
36	¶ 86; ¶ 87; ¶ 90; ¶ 91; Example 1; and the original claims
37	¶ 91; Example 1; and the original claims

Upon entry of this Amendment, claims 17-37 will remain pending in the application.

Because the foregoing amendments do not introduce new matter, entry thereof by the Examiner is respectfully requested.

II. Response to Issues Raised by Examiner in Outstanding Office Action

A. Claim Objections

Claim 15 is objected to for failing to recite the limitations of claim 1-11. In addition, claim 16 is objected to for being a method claim dependent on a composition claim. Office Action at page 3. Applicants respectfully traverse these objections as they may apply to the amended claims.

Claims 15 and 16 have been cancelled, and new claims 17-37 are submitted. These new method claims explicitly state the limitations of the composition claims and are not dependent upon composition claims. Accordingly, withdrawal of these objections is respectfully requested.

B. Claim Rejections - 3 U.S.C. § 112, Second Paragraph

Claim 16 is rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regard as the invention. Office Action at pages 3-4. Applicants respectfully traverse this rejection as it may apply to the amended claims.

The Examiner alleges that claim 16, a method claim, is indefinite for being dependent upon a composition claim. Without acquiescing to the rejection, claim 16 has been canceled and replaced with new method claims that are not dependent upon composition claims. Therefore, withdrawal of the rejection is respectfully requested.

C. Claim Rejections - 35 U.S.C. § 112, First Paragraph

1. Written Description

Claims 15 and 16 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Office Action at pages 4-7. Applicants respectfully traverse this rejection as it may apply to the amended claims.

The written description requirement for a claimed genus can be satisfied, *e.g.*, (a) by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, (b) by functional characteristics coupled with a known or disclosed correlation between function and structure, or (c) by a combination of such identifying characteristics, sufficient to show that the Applicants were in possession of the claimed genus. *See Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398, 1406 (Fed. Cir.. 1997).

The Examiner alleges that the claims are drawn to a method of treating a patient for multiple sclerosis comprising administering to a patient human interferon-β mutein. The Examiner further alleges that the scope of the claims encompass a genus of all possible muteins with function. Additionally, the Examiner states that "[t]he specification discloses interferon-β substitution at wild-type position 17 (C17S) and the deletion of the N-terminal

methionine of the human polypeptide . . . This meets the written description and enablement provisions of 35 USA 112, first paragraph." Office Action, page 5.

Applicants would like to draw the Examiner's attention to the final clause of the independent claims 17 and 26, which states "wherein said IFN-β mutein has a cysteine at position 17 deleted or replaced by a neutral amino acid." This limitation was found in the claims as originally filed and examined, and therefore it is not a new limitation introduced in the present amendment. As the claims require that the mutein have a specific mutation, namely a deletion or substitution by a neutral amino acid at Cys17 (using the wild-type amino acid numbering), the claims do not encompass "all possible muteins" as alleged by the Examiner. *See* Office Action, page 5. Instead, the claims encompass IFN-β muteins with a specific substitution or deletion at position 17. Such a feature provides for the common structural element to identify characteristics of the claimed genus. Indeed, the Examiner stated as much when making the statement ""[t]he specification discloses interferon-β substitution at wild-type position 17 (C17S) and the deletion of the N-terminal methionine of the human polypeptide . . . This meets the written description and enablement provisions of 35 USA 112, first paragraph." *Id.* It should be noted that the IFN-β muteins with or without the N-terminal methionine is described throughout the specification, *e.g.*, ¶ 18.

Further, the claims require that the IFN-β mutein be therapeutically effective for the treatment of multiple sclerosis (MS), thereby giving the encompassed muteins a common function that can be readily ascertained using the techniques disclosed in the specification, such as in Example 1. Therefore, because both structural and functional characteristics are well-described in the specification, as acknowledged by the Examiner in the Office Action. Accordingly, the written description requirement has been met and withdrawal of this ground for rejection is respectfully requested.

2. Enablement

Claims 15 and 16 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for all interferon-β mutein polypeptides. Office Action at pages 7-10. Applicants respectfully traverse this rejection as it may apply to the amended claims.

A proper analysis of the enablement requirement of 35 U.S.C. § 112, first paragraph, begins with a determination of the subject matter encompassed by the claims. *See* MPEP § 2164.08 ("All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner determine exactly what subject matter is encompassed by the claims.")

In this rejection, the Examiner asserts that the claims are drawn to "a method of treating a patient for multiple sclerosis comprising administering to a patient human interferon-β mutein." Office Action, page 7. However,the present claims are actually drawn to a method of treating a patient for multiple sclerosis comprising administering a pharmaceutical composition comprising an IFN-β mutein *with a deletion or substitution of Cys17 with a neutral amino acid.* The Examiner states that such muteins are enabled on page 7 of the Office Action, though the N-terminal deletion is mentioned, as well. The presence or absence of the N-terminal methionine is not fatal to enablement, since this deletion is well known in the art, as discussed in the specification and noted in Table 1 of the Giovannoni reference cited by the Examiner on page 11 of the Office Action.

The Examiner further alleges that there is insufficient structural and functional properties of the IFN-β mutein used in the claimed invention. However, the claims recite that the IFN-β mutein must have a deletion or substitution of a particular type at position 17. Further, the mutein must be therapeutically effective for the treatment of MS, which is defined in the specification beginning in ¶ 38. A person of skill in the art has ample guidance in the specification for practicing the claimed invention.

As acknowledged by the Examiner, the claims are fully enabled. Therefore, Applicants respectfully request that the rejection be withdrawn.

D. Claim Rejections - 35 U.S.C. § 102

Claims 15 and 16 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gottesman (abstract published 3/2003, Reference 8 in PTO 1449 of 07/06/2005) as evidenced by Giovannoni, *et al.*, *J. Neurol. Neurosurg. Psychiatry*, 73:465-469 (2002). Office Action at pages 10-11. Applicants respectfully traverse this rejection as it may apply to the amended claims.

An anticipation rejection under 35 U.S.C. § 102 requires a showing that each limitation of a claim is found in a single reference, practice or device. *See In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985). For a reference to be anticipatory, it must "be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention." *See In re Paulson*, 30 F.3d (Fed. Cir. 1994). The cited references do not anticipate the claimed invention as they do not teach each and every element of the claims.

As the Examiner discusses on page 11 of the Office Action, Gottesman teaches the administration of 500 μg of Betaseron to treat MS, and Giovannoni refers to an IFN-β mutein lacking an N-terminal methionine. However, the claimed invention recites that the IFN-β mutein is administered in amounts greater than 500 μg up to about 1000 μg (claim 17 and dependents), or greater than 500 μg to about 625 μg (claim 26 and dependents). Thus, Gottesman and Giovanoni fall outside the claims and cannot anticipate them. Therefore, Applicants respectfully request that the rejection be withdrawn.

E. Claim Rejections - 35 U.S.C. § 103

Claims 15 and 16 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gottesman as evidenced by Giovannoni (both previously cited) in view of Shirley et al. (U.S. Pat. No. 6,887,462). Office Action at pages 12-14. Applicants respectfully traverse this rejection as it may apply to the amended claims.

The Supreme Court has recently reaffirmed the *Graham* factors for the determination of obviousness. *See KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S. April 30, 2007). These four factual inquiries under *Graham* are: 1) determining the scope and contents of the

prior art; 2) ascertaining the differences between the prior art and the claims in issue; 3) resolving the level of ordinary skill in the prior art; and 4) evaluating evidence of secondary consideration. *Graham v. John Deere*, 383 U.S. 17-18 (1966). Here, the differences between the prior art and the present claims are so substantial that the cited art cannot render the present claims unpatentable.

The deficiencies of Gottesman in view of Giovannoni is discussed *supra*, namely that the dosage taught by these references falls outside the scope of the claimed invention. Shirley does not remedy that deficiency as it does not disclose a method of treating a patient for multiple sclerosis comprising administering a pharmaceutical composition comprising a dosage greater than either 500 μg up to about 1000 μg, or greater than 500 μg to about 625 μg, of a IFN-β mutein with a deletion or substitution of Cys17 with a neutral amino acid. Shirley merely discloses IFN-β compositions without human serum albumin. Thus, the combination of Gottesman, Giovannoni and Shirley does not arrive at the claimed invention, and therefore cannot render the claimed invention obvious.

Because a *prima facie* case for obviousness has not been met, Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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